

**MRI-based Investigation into the Effects of Simulated Microgravity on Cerebrospinal  
Fluid and Vascular Flow**

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**MRI-Based Investigation into the Effects of Simulated Microgravity on Cerebrospinal  
Fluid and Vascular Flow**

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## **LIST OF SYMBOLS AND ABBREVIATIONS**

CSA	Cross Sectional Area
CSF	Cerebral Spinal Fluid
HDT	Head Down Tilt
ICP	Intracranial Pressure
IJV	Internal Jugular Vein
LBNP	Lower Body Negative Pressure
MOS	Microgravity Ocular Syndrome
MRI	Magnetic Resonance Imaging
NASA	National Aeronautics and Space Administration
ONS	Optic Nerve Sheath
ROI	Region of Interest
VIIP	Visual Impairment and Intracranial Pressure Syndrome



## Summary

National Aeronautics and Space Administration (NASA) astronauts have reported decrease in visual acuity due to Microgravity Ocular Syndrome (MOS) after returning from long duration space missions. It is hypothesized that MOS results from a head-ward fluid shift induced by the effects of microgravity. This shift increases intracranial pressure (ICP) resulting in optic nerve damage and visual impairment (Gerlach et al., 2017). Previous studies on MOS have examined Magnetic Resonance Imaging (MRI) scans of subjects on earth under simulation of microgravity. These studies have utilized the proportionality between posture and intracranial pressure in the Head Down Tilt (HDT) protocol for simulating the effects of microgravity. The protocol consists of two scans: a baseline scan in the supine position ( $0^\circ$ ) and a head down tilted scan at a specific angle for comparison. We used the MRI scans conducted at Emory University's Center for Systems Imaging to analyze changes in arterial and venous blood flow under simulations of microgravity. Ten healthy volunteers underwent two MRI scans: one scan at a HDT of  $-15^\circ$  to simulate the effects of microgravity and another scan in the supine position ( $0^\circ$ ) to serve as a baseline for comparison. Results from the scans showed a decrease in arterial blood flow in the HDT position but no change in venous blood flow in the HDT position.

## **Chapter 1**

### **Introduction**

Upon returning from long duration space missions, National Aeronautics and Space Administration (NASA) astronauts have reported decrease in visual acuity due to Microgravity Ocular Syndrome (MOS). The leading hypothesis behind the cause of MOS is an increase in intracranial pressure (ICP) due to a head-ward fluid shift induced by the effects of microgravity (K. Marshall-Goebel et al., 2016). Earlier research has shown that gravity plays an essential role in balancing intracranial pressure. On earth, gravity functions to pull the fluids in our bodies (specifically, blood and cerebral spinal fluid) downwards; however, in the absence of gravity, these fluids pool inside the skull causing an increase in intracranial pressure (Roberts et al., 2015). This increase in pressure may cause damage to the optic nerve resulting in visual impairments (Gerlach et al., 2017). Due to these risks, NASA has launched several clinical and research protocols to determine the mechanisms involved in MOS and develop a solution (Francisco, 2017).

Previous studies on MOS have utilized the Head Down Tilt (HDT) technique to simulate the effects of microgravity in subjects on earth, during Magnetic Resonance Imaging (MRI) scans. The HDT technique utilizes the proportionality between posture and intracranial pressure to simulate these effects (Holmlund, 2017). The method consists of subjects receiving an MRI scan while lying in the supine position ( $0^\circ$ ) and comparing it to the same subject's MRI scan while lying tilted (head down) at a specific angle. Studies have been performed at HDT angles of  $0^\circ$ ,  $-6^\circ$ ,  $-10^\circ$ ,  $-12^\circ$ ,  $-15^\circ$ ,  $-18^\circ$ , and  $-20^\circ$  (Ishida et al., 2017; Macias, 2015; K. Marshall-Goebel et al., 2016; Petersen, Petersen, Andresen, Secher, & Juhler, 2016; Watkins W, 2017). Recent studies have shown increases in ICP in HDT of  $-10^\circ$  and twice as much increase at HDT  $-20^\circ$

(Petersen et al., 2016; Watkins W, 2017). In HDT at  $-15^{\circ}$ , skull pulsations were used to measure ICP which showed a ~20% increase compared to supine position (Watkins W, 2017). The MRI images collected from studies at  $0^{\circ}$ ,  $-6^{\circ}$ ,  $-12^{\circ}$  and  $-18^{\circ}$  were examined for both the cerebral blood flow and cerebral spinal fluid (CSF) flow of astronauts in space (Ishida et al., 2017; K. Marshall-Goebel et al., 2016). Results from previous studies confirmed increased intracranial pressure in the HDT position. However, further research at additional angles of HDT is required to compare the accuracy of the simulated results to the pressures experienced by astronauts in microgravity.

Analysis of cerebral blood flow has resulted in discrepancies between previous studies on whether the effect of HDT protocol increases or decreases vascular flow (Ishida et al., 2017; Marshall-Goebel et al., 2016). The results from examination of CSF flow in subjects undergoing a HDT protocol have not determined the specific mechanisms involved in the flow of CSF (Francisco, 2017; Ishida et al., 2017; Marshall-Goebel et al., 2016; Roberts et al., 2015). Cerebral blood flow has been analyzed immediately and with a 4.5-hour stabilization period at HDT  $-6^{\circ}$ ,  $-12^{\circ}$ , and  $-18^{\circ}$ , but it has not been analyzed at HDT  $-15^{\circ}$  with a thirty-minute stabilization period. At HDT  $-15^{\circ}$ , a decrease in arterial blood flow is expected based on the results of previous studies while an increase in venous blood flow is expected based on the similar time duration as reported in previous studies (Ishida et al., 2017; K. Marshall-Goebel et al., 2016). Further, an increase in venous blood flow is expected due to previous  $-15^{\circ}$  HDT study measurements of increased internal jugular vein (IJV) cross sectional area (CSA) (Watkins W, 2017). Assuming velocity remains constant, venous flow should increase with CSA. Additionally, the IJVs are the main pathway for cerebral drainage after a change in posture to the HDT position so an increase in the IJVs is expected as an immediate response to HDT (Ishida et al., 2017).

Our current study investigates the simulated effects of microgravity by comparing the MRI images of subjects at the supine position to the HDT position of  $-15^{\circ}$ . The MRI scans will be analyzed at a collaborator's lab for changes in optic nerve sheath (ONS) diameter (demonstrated by the amount of CSF around the optic nerve) at  $-15^{\circ}$  HDT to determine compliance of the ONS. An increase in CSF around the optic nerve, causing an increase in ONS diameter, is expected in the HDT position due to a head-ward shift in fluid. The lab at the Georgia Institute of Technology and Emory University Hospital examined the MRI scans for analysis of arterial and venous blood flow in supine ( $0^{\circ}$ ) and  $-15^{\circ}$  HDT positions to follow up on the inconsistent results of previous studies as well as examine fluctuations in CSF flow in both positions. It is hypothesized that a decrease in arterial blood flow and an increase in venous blood flow will occur at  $-15^{\circ}$  HDT.

## **Chapter 2**

### **Literature Review**

Microgravity Ocular Syndrome (MOS), also known as Visual Impairment and Intracranial Pressure Syndrome (VIIP), has been cited as the source of a decrease in visual acuity among astronauts returning from space missions. Statistically 29% of astronauts report visual impairment after short term missions and 60% report visual impairment after long term missions (Gerlach et al., 2017). The National Aeronautics and Space Administration (NASA) has launched several clinical and research protocols to investigate the cause of MOS in astronauts and gain a better understanding of the mechanisms involved. Through this research, NASA intends to develop a solution to MOS to protect the vision and health of future astronauts (Francisco, 2017).

Currently, eye examinations are performed on each NASA astronaut before and after space flight to gauge the effects of space travel on an astronaut's vision (Francisco, 2017). Symptoms developed over the course of space flight can include choroidal folds, retinal nerve fiber layer thickening, hyperopic shifts, optic disc edema, and globe flattening (Kramer, Sargsyan, Hasan, Polk, & Hamilton, 2012; Mader et al., 2013). The symptoms found in MOS have commonality with the earth born condition, Idiopathic Intracranial Hypertension (IIH). IIH is characterized by increased intracranial pressure due to unknown reasons (Roberts et al., 2015).

#### **CSF Pressure**

As it is currently understood, CSF is produced in the choroid plexuses, flows through the third and fourth ventricles to the subarachnoid space, surrounding the brain and spinal cord. Small amounts of CSF enter the subarchnoid space surrounding the optic nerve and flow

continuously along the optic nerve (Gerlach et al., 2017; Killer et al., 2007). From this, researchers understand the path CSF takes in the body, but the mechanism of how CSF is increased in the absence of gravity is unknown (Francisco, 2017; Gerlach et al., 2017).

Previous research into MOS has hypothesized the sustained increase in intracranial pressure as the leading cause of the visual impairment. The increase in intracranial pressure is caused by a buildup of cerebral spinal fluid in the skull under the absence of gravity. Studies simulate microgravity with the Head Down Tilt technique (HDT) by utilizing wedges built at specific angles and having volunteer subjects lay head down on the wedge, allowing the fluid in their body to pool in their head. MRI images are then analyzed for pre-and post HDT to determine the increase in pressure caused by the simulation of microgravity (Gerlach et al., 2017; Ishida et al., 2017; K. Marshall-Goebel et al., 2016).

#### CSF and Blood Flow in HDT

Several factors have been investigated for their effect on the increase in pressure such as cerebral spinal fluid flow, blood flow, percent CO<sub>2</sub>, time lapse, and the degree of angle on the wedge for simulation of microgravity. In 2016, Karina Marshall-Goebel studied MRI images taken with the HDT technique at 0°, -6°, -12°, and -18° analyzing both blood flow and CO<sub>2</sub> percentage. The findings from this study suggest HDT simulation leads to symptoms of MOS through venous congestion examined by decreases in total arterial blood flow and a correlation between increases in the internal jugular veins' cross-sectional area and the degree of head down tilt. Additionally, the results showed an increase in total arterial blood flow with increased CO<sub>2</sub> percentages. (K. Marshall-Goebel et al., 2016).

A follow up study conducted in 2017, focused on cerebral spinal fluid flow and the application of lower body negative pressure to reduce the effects of the HDT simulation. The study found that applied negative pressure minimized the increase in intracranial pressure and is a viable option for further exploration (K. T. Marshall-Goebel, Robert; Gerlach, Darius; Kuehn, Simone; Mulder, Edwin; Rittweger, Jorn, 2017).

Similarly, another study conducted in 2017 utilized phase-contrast MRI images taken at head-down tilt angles of  $0^{\circ}$ ,  $-6^{\circ}$ , and  $-12^{\circ}$  to analyze the fluctuations in cerebral spinal fluid flow, pressure gradient, and intercranial compliance index. In contrast to the results of the 2016 study by Karina Marshall-Goebel, this study discovered an increase in venous outflow in relation to the HDT degree but little change in the overall parameters of blood flow and physiology due to the low tilt angles and short time durations of the study. Both studies only measured the IJVs for venous flow and measured the internal carotid arteries and vertebral arteries for arterial flow. The 2017 study called attention to the importance of stabilization time before HDT as a key variable in determining the significance of results. Discrepancies in the results with previous studies were hypothesized to be due to a difference in time volunteers were required to lay in the HDT position (Ishida et al., 2017). Table 1 compares the parameters and results of the two studies.

Marshall-Goebel vs. Ishida Study				
	Position	Time (hrs)	Arterial	IJVs
Ishida	6°	0	ns	ns
	12°	0	decrease	increase
Marshall - Goebel	6°	4.5	decrease	ns
	12°	4.5	decrease	decrease
	18°	4.5	decrease	ns

**Table 1:** Comparison of Marshall-Goebel 2016 study vs. Ishida 2017 study (ns = non-significant result)

### Effect on HDT Angle

Studies have been conducted at several different angles to determine the optimum HDT angle for simulation of gravity. A 2015 study utilizing -15° HDT with five-minute stabilization periods found significant increases in intraocular pressure compared to the supine position. The study also saw reductions in intraocular pressure when low body negative pressure (LBNP) was applied for ten minutes in the HDT position (Macias, 2015). Another 2017 study performed at -15° HDT also used five-minute stabilization periods followed by ten minutes of LBNP. This study used skull pulsations to noninvasively measure ICP and found a 20% increase in ICP at -15° HDT. Other results showed increases in IJV CSA and ICP in the HDT position that were reduced by LBNP (Watkins W, 2017).

A 2015 study investigating the effects of posture on intracranial and cerebral pressure found ICP in relation to postural changes was dominated by venous pressure. It was determined that in upright posture positions from 10°-30°, the neck veins collapse to prevent the brain from exposure to negative pressures. However, in HDT positions simulating the effects of microgravity, the neck veins remain open where venous pressure can be transferred to the brain. This study examined HDT at -20° and found ICP changes in relation to short-term postural



changes depend on venous drainage while cerebral perfusion pressure is maintained in any postural position by the regulation of systemic arterial blood pressure (Petersen et al., 2016).

Based on prior research, NASA has selected a HDT protocol with an angle of  $-15^{\circ}$  as the optimum simulation to be used in microgravity research protocols. A stabilization period of 30 minutes has been selected based on previous data demonstrating head-ward fluid shifts increasing choroidal volume over 30 minute time periods (Macias, 2015). On earth, gravity actively pulls the fluid down, but it is unknown how the fluid flows up in the presence of gravity. Furthermore, the symptoms of MOS have not been present in all astronauts, leading researchers to question if the syndrome is related to an unknown biological response where certain individuals are predisposed (Francisco, 2017; Taibbi, Cromwell, Kapoor, Godley, & Vizzeri, 2013). In order to fully understand the problem and to develop a solution, it is necessary to determine the mechanisms involved in CSF flow both on earth and in space.

The overall study investigates changes in ONS diameter before and after HDT of  $-15^{\circ}$ . In the sub-study presented here, we will analyze arterial, venous, and CSF flow. Through analysis of vascular blood flow in the supine and  $-15^{\circ}$  HDT position, this study will address discrepancies in previous studies on the effects of HDT position in relation to blood flow. By analyzing changes in ONS diameter, fluctuations in CSF, arterial, and venous flow, the long-term aim is to determine material properties of the ONS and the mechanisms involved in fluid flow in the body.

## **Chapter 3**

### **Materials and Methods**

MRI scans followed the protocol attached in the appendix which was developed specifically for this study with a duration of approximately two hours. Volunteers gave written informed consent before removing all metal from their clothing and body and entering the room containing the MRI scanner. Two scans were performed on the volunteers, one in the supine position and a second in the Head-Down Tilt position.

#### **Scan 1 - Supine Position**

The volunteer laid in the supine ( $0^\circ$ ) orientation on the scanner table with a pulse monitor attached to the volunteer's finger. The volunteer rested in this position outside of the scanner for approximately 10 minutes before being prepped to enter the scanner. Ear plugs, a call button, and headphones were provided to the volunteer and foam was placed around the volunteer's head to ensure minimum movement during the scan. The 20-channel head coil was then locked in place with the coil element line on the coil aligned with the top of the volunteer's eyebrows as shown in Figure 1. The volunteer was reminded not to fall asleep during the scan and directed to stare at a cross hair projected in the mirror of the head coil to minimize eye movement. The scan lasted approximately 30 minutes.



**Figure 1:** Volunteer in supine position with eyebrows aligned with head coil.

#### Scan 2 – Head Down Tilt Position

Once scan 1 was complete, the volunteer was pulled out of the scanner and their blood pressure was taken. The subject then stood up while the scanner table was transformed to accommodate the head down tilt position and remained standing for approximately 1 minute before laying down in head down tilt position. A three-part wedge created out of pink foam and duct tape was assembled to create one large  $-15^{\circ}$  wedge as shown in Figure 2.



**Figure 2:** Foam block and two foam wedges are put together to form one -15° wedge.

A mat was placed on the wedge to provide further comfort for the volunteer and their head was placed in the same position as scan 1 with their eyebrows aligned with the line on the head coil. The pulse monitor was reattached to the volunteer's finger and the volunteer rested in this position outside of the scanner for approximately 30 minutes before starting the scan. The cross hair was adjusted to be in relatively the same position of eyesight for the volunteer as it was in scan 1 before the volunteer was inserted into the scanner as shown in Figure 3. Scan 2 took approximately 30 minutes and the volunteer's blood pressure was recorded after the scan.



**Figure 3:** Volunteer elevated at -15° inserted in MRI.

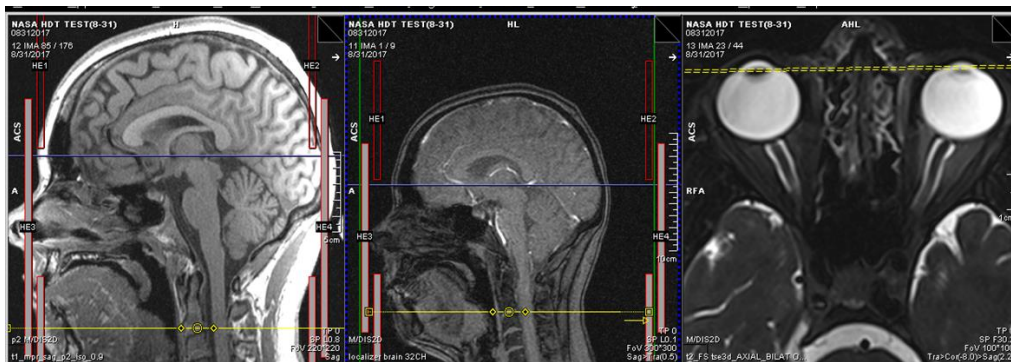
### Acquired Images

The same images were acquired for both scan 1 and scan 2 for comparison between the two positions. The following scans were performed for both positions:

- 1) Localizer Brain 32CH

- 2) T1\_mpr\_sag\_iso\_0.9
- 3) T2\_FS\_tse3d\_axial\_bilat orbit
- 4) T2\_FS\_tse3d\_COR\_ONS\_RT
- 5) T2-FS\_tse3d\_COR\_ONS\_LT
- 6) TRANS CSF Flow 10@C2
- 7) TRANS Blood Flow 80@C2-3
- 8) TOF\_FL2D\_TRA\_P2\_0006

The images consisted of peripheral pulse gated scans aligned perpendicular to the spinal cord and planned on the mid-sagittal T1 at the middle portion of the C2 vertebrae as shown in Figure 4. The parameters displayed in Table 2 stayed consistent throughout the scanning process.



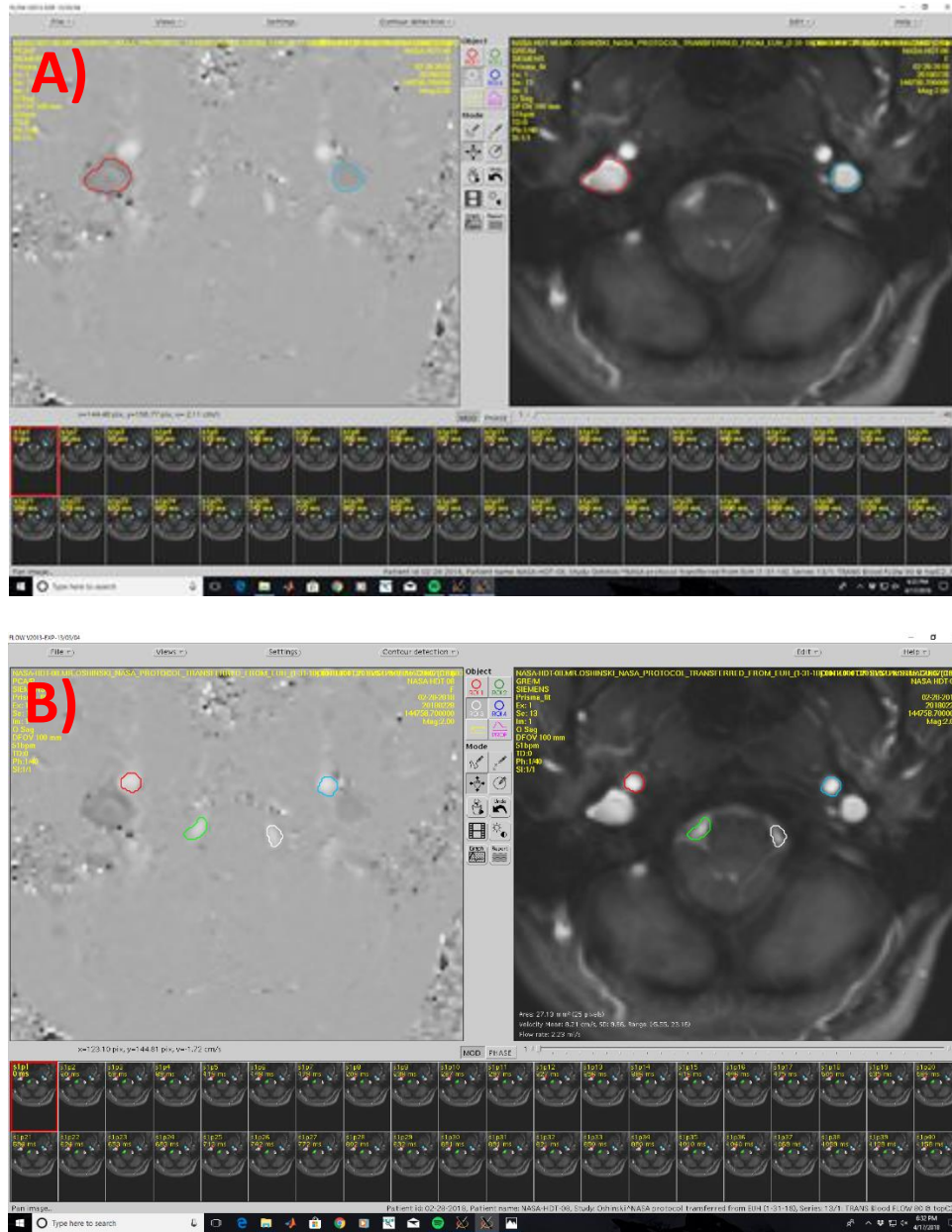
**Figure 4:** Images acquired on the mid-sagittal T1 at middle portion of C2 vertebrae.

Image Acquisition Parameters	
Scan Type	Phase Contrast
Pixel Resolution	192 x 192
Image Resolution	1m x 1m x .005m
Field of View	200 mm
Number of Cardiac Phases	40 nr phases
Echo Time	6.97 ms
Repetition Time	21.76 ms
Velocity in Coding Value	CSF: 10 cm/s
	Blood Flow: 80 cm/s

**Table 2:** Image parameters and specifications remained constant throughout both scan 1 and scan 2.

### Image Analysis

Images were analyzed for vascular flow rates using the program FLOW (AZL, Lieden the Netherlands). Regions of interest were outlined to obtain the area of the vein or artery using FLOW which utilized point by point velocity measurements to generate flow rates over 40 different time points throughout the scan in units of ml/s. Venous flow rates were acquired from the two internal jugular veins while arterial flow rates were acquired from the internal carotid artery and vertebral artery as shown in Figure 5. As could be seen in the phase images on the left in Figure 5, dark areas represent veins as they have negative flow rates where as white areas represent arteries as they have positive flow rates. Stroke volume was calculated using the generated stroke volumes for each ROI provided by the program FLOW. Arterial stroke volume of each subject was calculated by summing the stroke volumes from the four arteries (two internal carotid arteries and two vertebral arteries) ROIs while venous stroke volume was calculated by summing the stroke volumes from the two internal jugular vein ROIs.



**Figure 5:** A) internal jugular vein ROIs B) internal carotid artery and vertebral artery ROIs

All flow rates were normalized according to subject's body surface area (BSA) calculated by the Mosteller Formula ( $W$  = weight,  $H$  = height) (Mosteller, 1987).

$$BSA = 0.0167 \times W^{0.5} \times H^{0.5}$$

## Chapter 4

### Results

All volunteer data concerning physical characteristics of the volunteer is compiled in Table 3 in addition to pre and post head down tilt measurements of blood pressure and heart rate. Blood pressure was not recorded for volunteer 3 after the HDT position. Blood pressure was not measured for volunteers 6-10 after HDT scans due to switching to a MRI scanner that did not have a blood pressure monitor present.

Volunteer Information									
Volunteer #	Gender	Height in.	Weight lbs.	BSA m <sup>2</sup>	Age	Blood Pressure		Heart Rate	
						Supine	HDT	Supine	HDT
1	M	5'9	180	1.99	22	120/67	115/65	56	57
2	F	5'6	125	1.62	23	104/60	112/73	63	66
3	F	5'1	135	1.62	20	93/68		64	62
4	F	5'3	120	1.56	19	92/48	100/68	52	52
5	M	5'8	195	2.06	23	115/61	135/80	63	63
6	F	5'10	138	1.6	30			48	48
7	F	5'7	132	1.68	57			74	65
8	F	5'5	108	1.5	21			50	62
9	M	5'10	160	1.89	57			51	55
10	F	5'7	180	1.96	22			51	54

**Table 3:** Compiled volunteer data (height, weight, BSA, age, blood pressure, and heart rate).

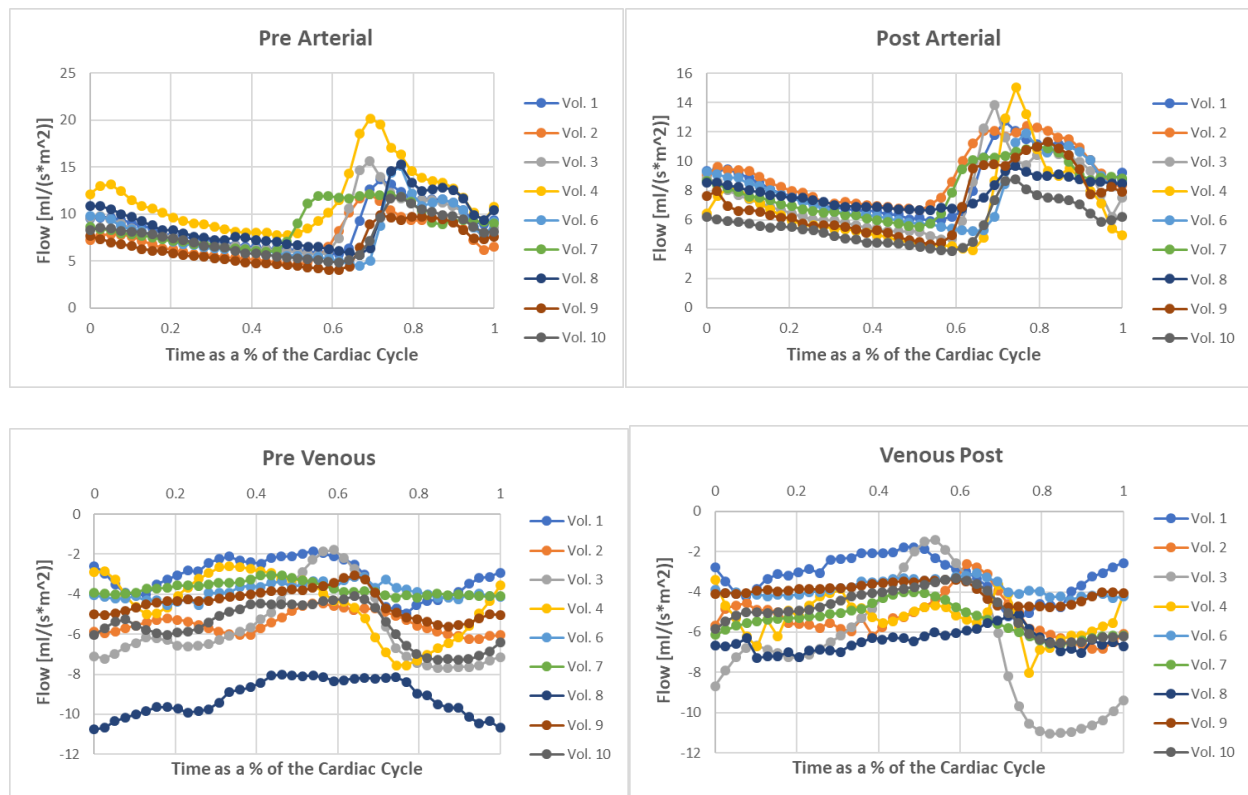
Heart rate on average showed an increase in the HDT position; however, the standard deviation between volunteers was high in both pre and post measurements as shown in Table 4. A paired t-test performed to measure statistical significance of the change in heart rate from pre to post HDT gave a p-value of 0.08.



Heart Rate		
	Pre	Post
Average	56	59
Standard Deviation	8.38	6.28

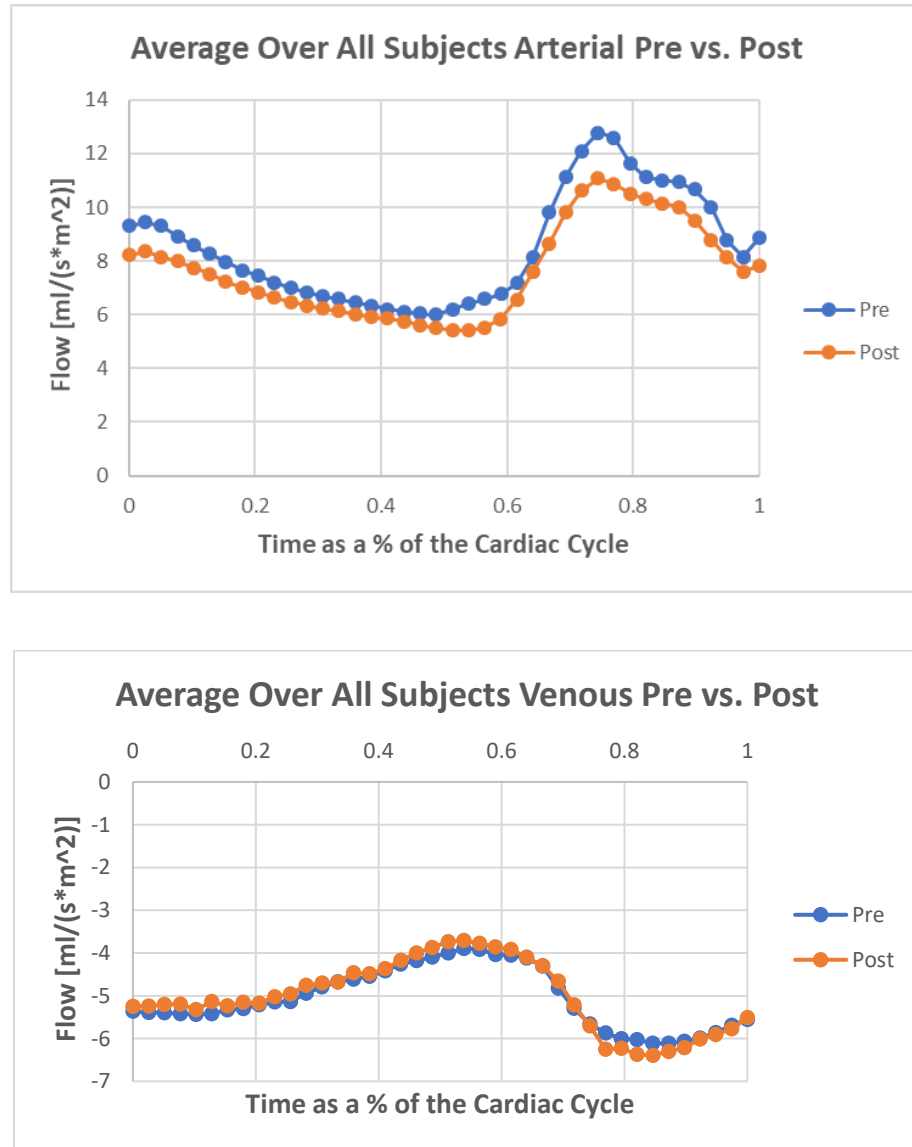
**Table 4:** Pre and post average heart rate and associated standard deviation.

Arterial and venous blood flow was analyzed and compiled into graphs comparing similarities of all volunteer's pre and post blood flows (Figure 6). Arterial blood flow followed a trend whereas venous blood flow showed more variation between subjects.



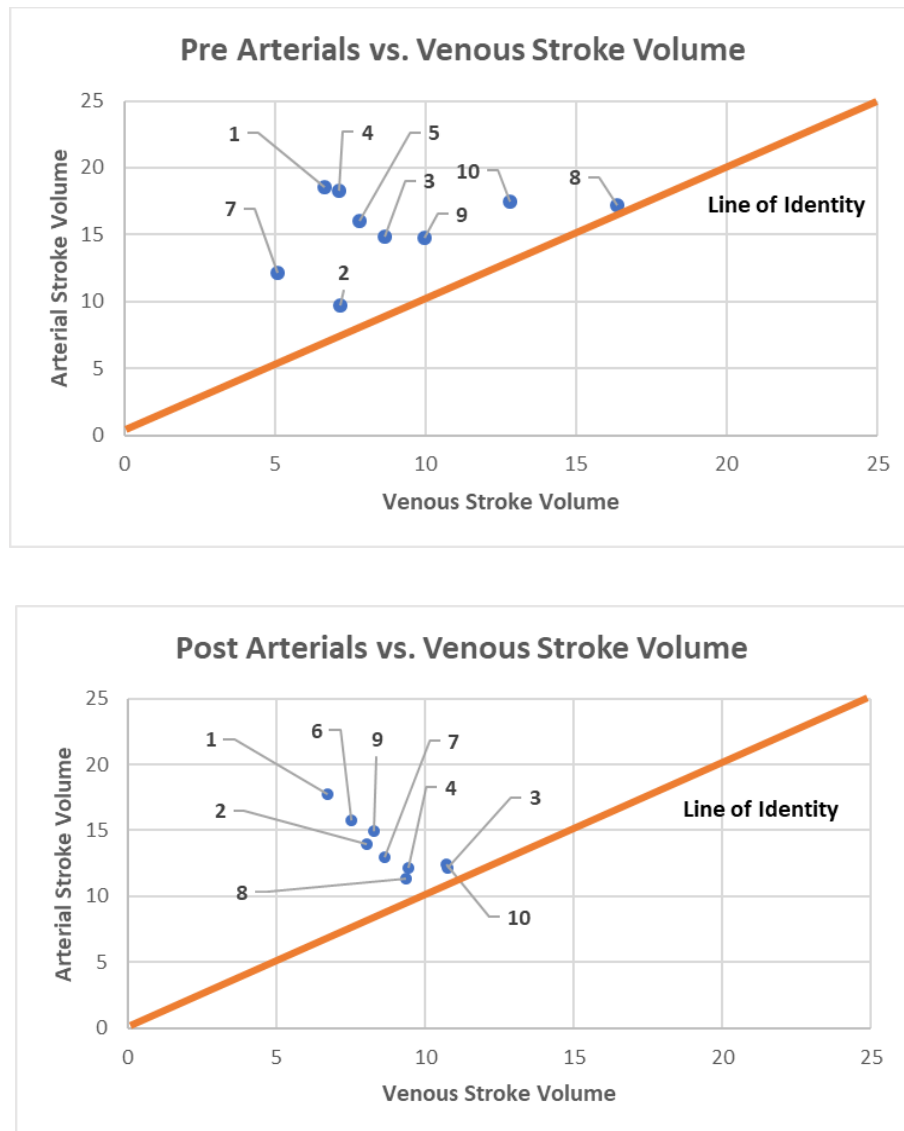
**Figure 6:** All volunteers' pre and post arterial and IJV blood flow plotted for comparison (Volunteer 5 excluded due to change in position during image acquisition between pre to post).

All subjects' arterial and IJV flow rates were averaged and compared for pre and post HDT as shown in Figure 7. Arterial flow decreased in the HDT position where as IJV flow showed no significant difference between pre and post HDT measurements.



**Figure 7:** Arterial and IJV pre vs. post averaged over all subjects (Volunteer 5 excluded due to change in position during image acquisition between pre to post). Standard deviation bars are not shown to display means more clearly.

Paired two sample for means t-tests were performed on the arterial and venous stroke volumes pre and post head down tilt to determine statistical significance of the HDT. The difference in arterial flow from pre to post resulted in  $p = 0.08$  and venous flow from pre to post resulted in  $p = 0.40$  as determined from the arterial and venous stroke volume data. The arterial stroke volumes were graphed against the venous stroke volumes for both the pre and post as shown in Figure 8. Ideally, if all venous flow was accounted for, points should fall along the line of identity to show equal inflow and outflow of blood; however, arterial stroke volumes were constantly larger than venous stroke volumes in both pre and post HDT. This illustrates that multiple venous structures which are difficult to identify contribute to the venous outflow.



**Figure 8:** Arterial vs. venous (IJV) stroke volumes pre and post (Volunteer 5 excluded due to change in position during image acquisition between pre to post).

## **Chapter 5**

### **Discussion**

This present study was conducted to answer a discrepancy between two past studies regarding whether HDT protocol increases or decreases vascular blood flow (Ishida et al., 2017; Marshall-Goebel et al., 2016). We found that when subjects underwent a HDT of  $-15^{\circ}$  for 30 minutes, venous flow showed no change from pre to post HDT while there was a trend towards decrease in arterial flow. However, the values did not reach statistical significance at a level of  $p < 0.05$ .

Heart rate was measured for volunteer 1-10 and showed a trend of increasing heart rate in the HDT position with  $p = 0.08$  although some volunteers did not show any change in heart rate at all between the two scans. Arterial blood flow between each subject followed similar changes from pre to post HDT over the cardiac cycle while venous blood flow showed little similarities over the cardiac cycle between volunteers as shown in Figure 6. Figure 7 shows averaged data from all volunteers and plotted for arterials and venous pre vs. post. Arterial vessels show a decrease in flow in the HDT position in agreement with previous study results trending toward significance with  $p = 0.08$ . Venous shows no change from pre to post with  $p = 0.40$ . Further analysis on the venous blood flow pre and post is required to determine if HDT protocol results in a decrease or increase in vascular flow. This result could be due to the stabilization period of 30 minutes before image acquisition in HDT position. The Ishida 2017 study reported an immediate increase in venous flow due to sudden response to positional changes where as the Marshall-Goebel study reported in decreases in venous flow over a 4.5 hour period. The 30 minute stabilization period in addition to the increased angle of  $-15^{\circ}$  compared to  $-12^{\circ}$  may

result in a time period between these two studies providing results showing no change in venous flow.

Stroke volumes were analyzed for both pre and post arterials and venous flow. Ideally, the pre-arterial stroke volume should equate to the pre-venous stroke volume and the same for the post comparison. However, results consistently showed higher arterial stroke volumes in both pre and post scans as shown in Figure 8. This inconsistency may be due to ROI selection for the veins or image acquisition location of the veins.

### Future Work

This study intends to further examine ROI selection and re-evaluate image location before proceeding with more volunteers. Currently, there is an age discrepancy and probably not enough subjects to see significant differences from pre to post HDT. The future study plans to have 15 total volunteers as well as analyze for cerebral spinal fluid change between pre and post HDT in volunteers 1-15.

### Limitations

A limitation of this study is that most of the volunteers were in their early 20s which does not equate to the typical age of astronauts. The study could be improved by looking at an age group closer to that of astronauts as well as an even distribution of men and women. Blood pressure was only measured for volunteers 1-5 who experienced a decrease in blood pressure in the HDT position. The variation between each volunteer shown in the venous graphs may be due to incorrect selection of regions of interests (ROIs) during image analysis or simply variations in anatomy from subject to subject.

### Conclusion

In conclusion, arterial blood flow has shown a decrease in the HDT position ( $p=0.08$ ) in comparison to the supine position while venous blood flow has shown no change between pre to post in conflict with both debated studies. The inconsistency between arterial and venous stroke volumes seen in the study warrants further investigation.

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## APPENDIX

### **NASA MRI Head Down Tilt Protocol**

**I. Remove all metal from clothing and body before entering MRI scanner room.**

**II. Scan 1- Supine Position**

- 1) Lay volunteer in supine (0°) orientation on scanner table, attach pulse monitor to volunteer's finger, and properly position volunteer for maximum comfort.**

Volunteer shall rest in this position outside of scanner for 10 minutes.

- 2) Provide volunteer with ear plugs and call button. Place headphones on volunteer. Carefully, lock in the 20-channel head coil. Ensure the line on the coil (as shown by the arrow in image below) is lined up with the top of the volunteer's eyebrow line.**



**Image 1:** Volunteer in supine position with eyebrows aligned with head coil.

- 3) Turn on projector cross hair and attach mirror to head coil. Direct the volunteer to stare at projected dot then slowly enter volunteer into scanner.**

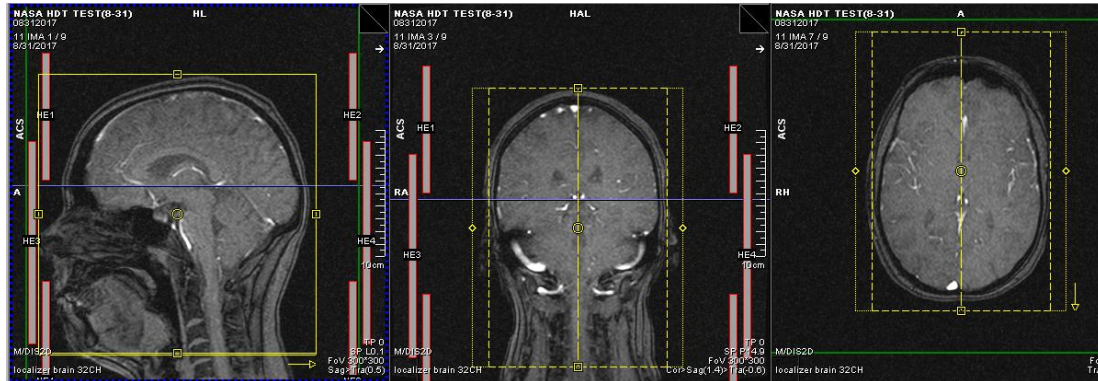
Remind volunteer not to fall asleep.

- 4) Begin scan. Scan will last approximately 30 minutes.**

**5) Run the following scans:**

- a. Localizer Brain 32CH**
- b. T1\_mpr\_sag\_iso\_0.9**

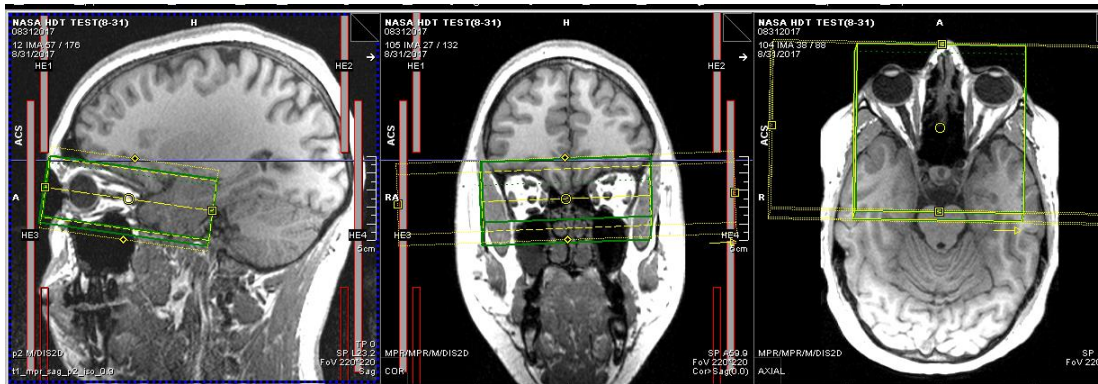
Plan to cover entire brain as shown in localizer images below. Do MPR of T1 Sagittal into transverse and coronal plane.



**Reformat Instructions:**

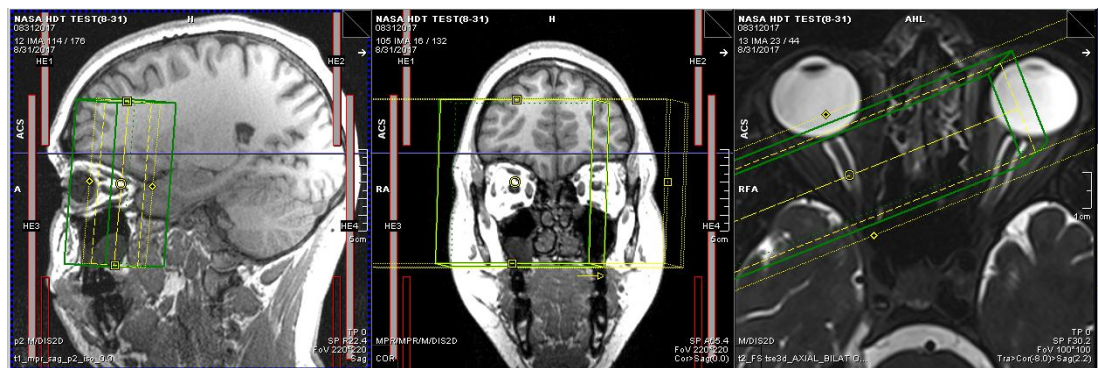
1. Select 3D and the icon for the images' anatomically correct orientation
2. Select parallel ranges then move the ranges to only acquire the area around the optic nerve
3. Enter 500 into the prompt for # of images
4. Select preview
5. Name the Range Series "axial plane"
6. Move the area to align over the optic nerve
7. Enter 500 into the prompt for # of images
8. Name the Range Series "coronal plane"
9. Click and drag new titles into the image screens
10. Move the area to align over the optic nerve

- c. T2\_FS\_tse3d\_axial\_bilat orbit**



Plan on sagittal T1, MPR transverse, and MPR coronal vein. Tilt to be in the plane of the optic nerve.

**d. T2\_FS\_tse3d\_COR\_ONS\_RT**

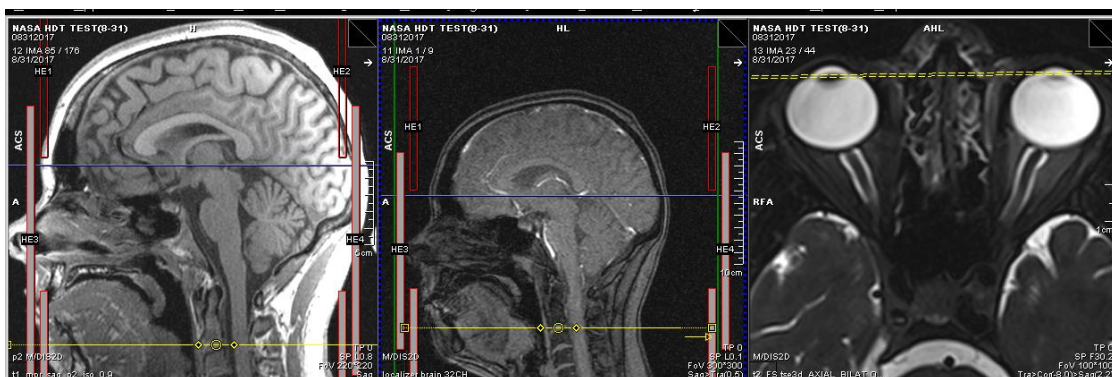


Plan perpendicular to optic nerve sheath. Begin scan volume 1mm inside globe. Center on coronal reformatted images over the globe.

**e. T2-FS\_tse3d\_COR\_ONS\_LT**

Same image as part d but on the left.

**f. TRANS CSF Flow 10@C2**



Plan on mid-sagittal T1 at middle portion of C2 vertebrae, align perpendicular to spinal cord.

**g. TRANS Blood Flow 80@C2-3**

Same image as part f but velocity increased from 10 to 80.

**h. DENSE mid-sagittal**

No tilting from sagittal.

**III. Scan 2- Head Down Tilt Position**

- 1) Once scan 1 is complete, pull volunteer out of scanner and take their blood pressure while they are still in the supine position.**

Set up machine to automatically take volunteers blood pressure every 15 minutes for the rest of the study.

- 2) Ask volunteer to stand up while you build wedge on scanner table.**

Place foam block at end of scanner table. Gaps in the bottom of the block should line up with table. Place foam wedge (15°) against end of foam block closest to scanner. Add second foam wedge on top of block to form one full body length wedge as shown below.

Build wedge as quickly as possible to limit total time volunteer is standing.

- 3) Lay volunteer on wedge.**

Insert cushions and pillows along wedge to provide maximum comfort to volunteer.



**Image 2:** Foam block and two foam wedges are put together to form one large 15-degree wedge.

- 4) Ensure the position of the volunteer's eyebrow line to the line on the head coil.
- 5) Attach pulse monitor to volunteer's finger. Volunteer shall rest for 30 minutes at incline of 15°.
- 6) Provide volunteer with ear plugs and emergency button. Place headphones on volunteer. Carefully, lock in the 20-channel head coil. Ensure the line on the coil is lined up with the top of the volunteer's eyebrow line.
- 6) Turn on projector cross hair and attach mirror to head coil. Ensure the cross hair is in the same position relative to the volunteer's view as it was when laying in the supine position. Direct the volunteer to stare at projected dot then slowly enter volunteer into scanner.

Carefully insert the volunteer to make sure the volunteer's legs are not too close to top of scanner.





**Image 3:** Volunteer elevated at 15 degrees inserted in MRI.

**7) Begin scan. Scan will last approximately 30 minutes.**

Repeat scans taken in the supine position parts a-f.

**IV. Once scan 2 is complete, pull volunteer out of scanner and have volunteer get up from scanner table.**

Ensure volunteer sits up slowly and allows time for their body to reorient itself before standing up.

**V. Remove and put away all cushions and pillows from scanner table. Remove foam block and wedges from scanner table and store in back room.**

**VI. Escort volunteer from scanner room.**